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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/775,050	02/09/2004	Yu-Chan Chao	08919-103001 / 13A-900919	8997

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EXAMINER	
GUZO, DAVID	
ART UNIT	**PAPER NUMBER**
1636	

DATE MAILED: 03/22/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/775,050	CHAO, YU-CHAN	
	Examiner	Art Unit	
	David Guzo	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 December 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-45* is/are pending in the application.

4a) Of the above claim(s) *7-45* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Detailed Action

Claims 7-45 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 8/23/05.

Given applicant's amendment filed 12/30/05, all previous grounds of rejection are withdrawn. Applicant's arguments directed against said rejections are therefore moot. The following new grounds of rejection are necessitated by applicant's amendment.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-6 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant claims a recombinant baculovirus that infects permissive host cells (insect cells) without lyzing the permissive host cells, wherein the recombinant baculovirus contains an intact p35 gene, an exogenous nucleic acid sequence encoding a polypeptide which can be a fluorophore such as ECFP, EYFP, EGFP or DsRed. The claims read on a genus of recombinant baculoviruses with the recited properties.

Applicant, in the specification (p.1), defines a baculovirus that infects insect cells without lyzing the cells as meaning that "the majority (i.e., at least 50%) of the host cells infected with the baculovirus are not lyzed upon maturation of viral progenies." The recombinant baculoviruses were generated by constructing a specific recombinant baculovirus (vAB^{h}cmEpL) by homologous recombination between a plasmid, pAB^{h}cmEpL, and a linearized viral DNA of AcMNPV (vACRP23.Laz) and mutagenizing the virus with 5-bromodeoxyuridine (BrdU). Applicant isolated 11,603 clones and apparently isolated and characterized 20 clones (designated A1, A2, A3, C4, 1028, 1044, 1053, 1071, 1081, 1085, 1091, 1094, 3058, 3074, PN8, PN9, PN19, PN23, PN24, and PN121) which did not lyse the majority of the cells infected and had intact p35 genes. Applicant did not genetically characterize the mutant recombinant baculoviruses to ascertain what genetic changes were responsible for the observed phenotype of not lyzing the majority of infected permissive cells. It appears that applicant checked cell lysis only with Sf21 cells, which are permissive for AcMNPV. The instant disclosure provides an adequate written description for the 20 clones which do not lyse the majority of the permissive infected cells.

The written description requirement for a genus may be satisfied by sufficient description of a representative number of species by actual reduction to practice or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show that applicant was in possession of the claimed

invention. In the instant case, applicants have provided no correlation between the functional characteristics of the viruses (reduced cell lysis) and the structure of the viruses (i.e. what genetic features or mutations were responsible for the observed phenotype). Since the mutant recombinant baculoviruses were generated by random BrdU mutagenesis, the genomes of the baculoviruses could contain hundreds of different mutations, wherein any one mutation or combination of mutations could result in the observed phenotype. Without any knowledge of the genetic features the different baculoviruses have in common and without a correlation between said genetic features and the observed function of the baculoviruses, it must be concluded that applicant has not provided a written description of the claimed genus. While applicant has isolated 20 clones, this does not comprise a representative number of species because without additional information, each represents a unique clone with unknown genetic alterations which impart the recited functional properties. Possession of one clone would not put into the hands of the skilled artisan the other recited clones.

Claims 1-6 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the twenty clones designated A1, A2, A3, C4, 1028, 1044, 1053, 1071, 1081, 1085, 1091, 1094, 3058, 3074, PN8, PN9, PN19, PN23, PN24, and PN121, does not reasonably provide enablement for any recombinant baculovirus that infects permissive host cells without lyzing the cells and wherein the virus contains an intact p35 gene. The specification does not enable any person skilled

in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicant's invention is as described above.

The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the specification coupled with information known in the art without undue experimentation (*United States v. Telectronics*, 8 USPQ2d 1217 (Fed. Cir. I 988)). Whether undue experimentation is needed is not based upon a single factor but rather is a conclusion reached by weighing many factors. These factors were outlined in *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Inter. I 986) and again in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. I 988) and include the following:

1) Unpredictability of the art. The art in the area of developing recombinant baculoviruses which do not lyse infected permissive cells and have an intact p35 gene must be considered unpredictable. As applicant indicates in the instant specification, baculoviruses are well known to infect and lyse permissive cells. Applicant has used random mutagenesis (using BrdU) to generate at least 20 clones that exhibit a markedly reduced level of lysis of permissive Sf21 cells. Applicants do not provide any correlation between any specific genetic alterations in the genomes of these clones and their observed function of reduced cell lysis. It therefore must be considered unpredictable as to whether any given mutation, or group of mutations, in a baculoviral genome will result in the inability of the resultant baculovirus to lyse permissive host cells. Additionally, applicant used, as a starting virus, which was then mutated, the

vAB^{h}cmEpL virus, which was generated using a specific transfer vector and a specific linearized viral DNA of AcMNPV (vAcRP23.Laz). What role in the resultant properties of the baculoviral mutants the starting materials may have played is unknown.

2) Number of working examples. Applicant presents 20 AcMNPV clones with the recited characteristics.

3) State of the art. The art in the area of generating recombinant baculoviruses with intact p35 genes must be considered poorly developed as the art does not disclose any such viruses.

4) Amount of Guidance. Applicant provides guidance only in the generation of mutant clones from a single recombinant baculovirus (an AcMNPV) subjected to random mutagenesis using BdrU. The mutant clones only demonstrate reduced lysis in one permissive cell line (Sf21). Whether the reduced lysis is demonstrated in other cells permissive for replication of AcMNPV is unknown.

5) Scope of the invention. The scope of the invention is broad, as it reads on any recombinant baculovirus (there are hundreds of different baculoviruses) that infect permissive cells without lyzing said cells and having an intact p35 gene.

6) Nature of the invention. The invention involves the generation of recombinant baculoviruses with unique properties.

7) Level of skill in the art. The level of skill in the art is high.

Given the above analysis of the factors which the courts have determined are critical in ascertaining whether a claimed invention is enabled, it must be considered

that the skilled artisan would have had to have conducted undue and excessive experimentation in order to practice the claimed invention.

It is also noted that a deposit of the 20 clones disclosed by applicant are required. Said clones are required to practice the claimed invention and are not disclosed in the prior art or are commercially available. The skilled artisan would not be able to reliably reproduce the claimed clones as said clones were generated by random mutagenesis using BrdU and applicant has not characterized said clones at the molecular level so as to identify the specific mutations in the genomes of the baculoviral clones. A deposit of said clones is therefore required and applicants must comply with the requirements of 37 CFR 1.801-1.809.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 (and dependent claims) are vague in the recitation of the term "contains an intact p35 gene". It is unclear what an "intact p35 gene" encompasses. It is unclear if the p35 gene is mutated or wild-type since "intact" is not defined by applicant and it could potentially read on mutated or wild-type forms of the gene. Also, since the instant recombinant clones were generated by random mutagenesis, it is unclear if applicant means to recite that the p35 gene is not mutated, i.e. intact?

No Claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Guzo, Ph.D., whose telephone number is (571) 272-0767. The examiner can normally be reached on Monday7-Thursday from 8:00 AM to 5:30 PM. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel, Ph.D., can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

David Guzo
March 9, 2006

DAVID GUZO
PRIMARY EXAMINER